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PATENT  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appl. No. : 10/535,723  
Appellants : Manuel VANGELISTI  
Filed : May 20, 2005  
Title : NOVEL PROCESS FOR THE PREPARATION OF 2-AMINOMETHYLPYRIDINE DERIVATIVE  
TC/A.U. : 1625  
Examiner : Binta M. Robinson  
Docket No. : P/3610-59

Mail Stop Appeal Brief - Patents  
Commissioner of Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**APPELLANT'S APPEAL BRIEF**

Sir:

The above-identified Appellant submits this Appellant's Appeal Brief pursuant to 37 C.F.R. § 41.37(d). The Notice of Appeal was filed on October 11, 2007.

Please charge the official fee of \$510 for filing a brief in support of an appeal to our Deposit Account Number 15-0700. A duplicate copy of this page is enclosed.

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**CONTINGENT EXTENSION REQUEST**

If this communication is filed after the shortened statutory time period had elapsed and no separate Petition is enclosed, the Director of Patents and Trademarks is petitioned, under 37 C.F.R. § 1.136(a), to extend the time for filing a response to the outstanding Office Action by the number of months which will avoid abandonment under 37 C.F.R. § 1.135. The fee under 37 C.F.R. § 1.17 should be charged to Deposit Account No. 15-0700.

The Appellant relies upon the following authorities and arguments to maintain the appeal.

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**1. Real Party in Interest**

The real party in interest for this matter is the Appellant's assignee. The assignee and real party in interest is Bayer Cropscience S.A., F-69009 (FR).

**2. Related Appeals and Interferences**

There are no other appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**3. Status of Claims**

Claims 2 through 8 and 11 through 14 are pending in the application and are rejected and appealed..

**4. Status of Amendments**

No amendments were filed subsequent to the final rejection by the Examiner. Therefore, the attached listing of claims reflects the claims proposed at the time of the final Office Action of July 11, 2007.

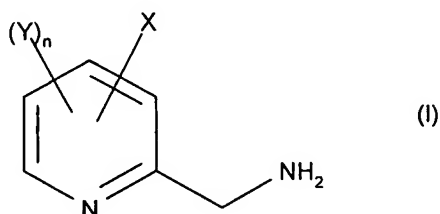
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5. Summary of Claimed Subject Matter

In one embodiment detailed in the specification on page 1, line 2 through page 2, line 9; and page 3, lines 1 through 22; the present invention is directed to a process for the preparation of a 2-aminomethylpyridine derivative of general formula (I)

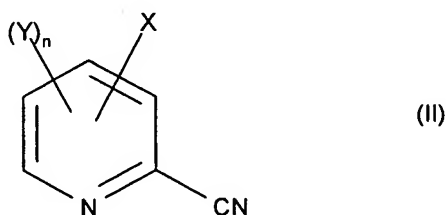


wherein

n represents 0, 1, 2 or 3,

X is a halogen atom,

each Y, which may be the same or different, is selected from the group consisting of a halogen atom, halogenoalkyl, alkoxycarbonyl, and alkylsulphonyl, or a salt thereof; comprising hydrogenating a 2-cyanopyridine derivative of general formula (II):



in which n, X, and Y are as described above,

in acetic acid using Raney nickel, at a temperature of from 30°C to 70°C, under a hydrogen pressure of from 10 to 20 bar.

In preferred embodiment detailed in the specification on page 3, lines 24 through 29, the present invention is directed to a process for the preparation of 2-aminomethyl-3-chloro-5-trifluoromethylpyridine comprising hydrogenating 3-chloro-2-cyano-5-trifluoromethylpyridine in acetic acid using Raney nickel introduced in a weight ratio of from 1 to 20% with respect to the 3-chloro-2-cyano-5-trifluoromethylpyridine, at a temperature of from 40 to 50°C, under a hydrogen pressure of from 15 to 20 bar.

**6. Grounds of Rejection to Be Reviewed on Appeal**

Claims 2 through 8 and 11 through 14 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Dann et al. (WO 0216322) in view of Rylander (Catalytic Hydrogenation in Organic Synthesis, Academic Press, 1979, page 140) or Frebault (Hcaplus 1906:119496).

**7. Argument**

**Examiner's 35 U.S.C. § 103(a) rejection of claims 2 through 8 and 11 through 14.**

The Examiner rejected claims 2 through 8 and 11 through 14 under 35 U.S.C. § 103(a) as unpatentable over Dann et al. (WO 0216322) in view of Rylander (Catalytic Hydrogenation in Organic Synthesis, Academic Press, 1979, page 140) or Frebault (Hcaplus 1906:119496).

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WO 02/16322 to Dann et al. discloses a process for the preparation of 2-aminomethylpyridine derivatives falling within the definition of the compound of formula (I) according to the present invention, by catalytic hydrogenation of 2-cyanopyridine derivatives falling within the definition of the compound of formula (II) according to the present invention. Nevertheless, the process disclosed in Dann et al. is a catalytic hydrogenation conducted in the presence of a catalyst chosen from a list of possible catalysts in which Raney nickel is not cited (*see* page 4, lines 1-2: Raney nickel is not cited). Furthermore, the use of acetic acid to perform the catalytic hydrogenation is not disclosed in Dann et al. (*see* page 4, lines 13-21: acetic acid is not cited).

Thus, even if Dann et al. disclose a process for preparing compounds similar to compounds of formula (I) according to the present invention by catalytic hydrogenation of similar starting material, the experimental conditions of these processes are totally different (catalyst, solvent, etc.).

As mentioned above, Dann et al. disclose a process for the preparation of 2-aminomethylpyridine derivatives falling within the definition of the compound of formula (I) according to the present invention, by catalytic hydrogenation of 2-cyanopyridine derivatives falling within the definition of the compound of formula (II) according to the present invention using a catalyst chosen as being palladium, platinum, ruthenium, nickel or cobalt (preferably palladium), in the presence of an alcohol solvent, at a temperature of from 0°C to 60°C (preferably of from 20°C to 30°C), under a hydrogen pressure of from 1 to 4 bar.

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The teaching of Dann et al. is clearly focused on the use of a palladium catalyst to prepare the compound of formula (I) starting from the compound of formula (II) (*see* page 4, lines 5-6 & Example 1, page 10). Palladium catalysts are well known by the ordinarily skilled artisan as facilitating by-product dehalogenation reactions. Furthermore, the teaching of Dann et al. clearly and strongly recommends the use of a catalyst inhibitor to improve selectivity of the reaction by limiting these dehalogenation by-product reactions (*see* page 4, line 29, to page 5, line 10). Thus, nothing in the teaching of Dann et al. discloses or even suggests the use of Raney nickel in acetic acid to prepare 2-aminomethylpyridine substituted by a halogen atom by catalytic hydrogenation of 2-cyanopyridine substituted by a halogen atom in acceptable yields at an industrial scale and avoiding the use of catalyst inhibitors which are expensive and difficult to be used in an industrial process to prevent by-product dehalogenation reactions.

Further, there is no disclosure or suggestion in Dann et al. of employing a pressure in the range of from 10 to 20 bar in the reaction.

Rylander discloses, *inter alia*, that the products of nitrile hydrogenation depend markedly on the catalyst and on whether the nitrile is aliphatic or aromatic. He teaches that nickel, nickel boride, and cobalt appear to be the best catalysts for converting low molecular weight *aliphatic* nitriles to primary amines, particularly when the reduction is carried out in ammoniacal methanol. He also states that *aromatic* amines on reduction give a mixture of benzylamines, dibenzylamines, and ring reduced products *that depend on catalyst, solvent, and reaction conditions*. (See page 141.) There is no disclosure of what such catalyst, solvent, or reaction

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conditions ought to be to obtain a desired end-product, nor any mention of carrying out the process in an acid, such as the acetic acid of the present invention.

Cyanopyridines, of course, are not aliphatic nitriles, but are aromatic nitriles, and Rylander mentions that the preferred catalysts for converting low aromatic nitriles to amino derivatives are platinum, rhodium, or palladium (see page 141). No mention is made of nickel catalysts.

Frebault discloses that primary and secondary aromatic amines can be obtained by the direct hydrogenation of aromatic nitriles in the presence of reduced nickel. Specifically, the reaction is carried out in a tube containing reduced nickel imbedded in iron filings, through which a rapid current of hydrogen is passed through at about 250° (presumably centigrade), while the nitrile is allowed to fall directly into the tube drop by drop, which does not sound like a commercially feasible process. The only nitriles mentioned are benzonitrile and *p*-tolunitrile, neither of which contain any ring-substituted halogen, which presents problems that are overcome by the present invention. Further, and again, there is no disclosure of carrying out the hydrogenation in the presence of an acetic acid solvent.

Neither Rylander nor Frebault were dealing with cyano/amino moieties that were substituted with a halogen atom, which is an essential feature of the present invention. Both references clearly state that when reducing benzonitrile (i.e., aromatic nitriles) into benylamine (i.e., aromatic amines), side-reaction products (i.e., di- or tribenzylamine) are generated in very high proportion. See page 141 of Rylander and the last sentence of Frebault. Such by-products



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are *not* generated using the process of the present invention. The last paragraph of the example of the present application shows that a 97% yield of 2-aminomethyl-3-chloro-5-trifluoromethyl pyridine over 3-chloro-2-cyano-5-trifluoromethylpyridine is obtained, which excludes production of side-products in high quantities. A process generating such high levels of by-products would not be acceptable on an industrial scale level and this would have discouraged the person of ordinary skill in the art from using the teachings of Rylander and/or Frebault.

Clearly, the secondary references fail to supplement the deficiencies of Dann et al., described above, as a reference.

**Conclusion**

The Examiner's cited references fail to disclose or make obvious the process claimed by the Appellant. These rejections should be reversed.

Favorable consideration of the application is respectfully requested.

**8. Claims Appendix**

An appendix is attached that contains a copy of the claims, as amended, that are involved in this appeal.

**9. Evidence Appendix**

The Appellant does not rely on additional evidence in this appeal.

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10. Related Proceedings Appendix

The Appellant is unaware of any related proceedings.

Respectfully submitted,



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**Claims Appendix**

**Listing of Claims:**

1. (Canceled)
2. The process of claim 13 wherein X is chlorine.
3. The process of claim 13 wherein n is 1.
4. The process of claim 13 wherein Y is haloalkyl.
5. The process of claim 4 wherein Y is trifluoromethyl.
6. The process of claim 13 wherein X is chlorine, n is 1 and Y is trifluoromethyl.
7. The process of claim 6 wherein the compound of general formula (I) is 2-aminomethyl-3-chloro-5-trifluoromethylpyridine.
8. The process of claim 13 wherein the temperature is in the range of from 35 to 50° C.

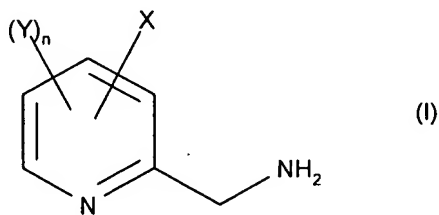
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9 - 10 (Canceled)

11. The process of claim 13 wherein the Raney nickel is introduced in a weight ratio of from 1 to 20% with respect to compound of general formula (II).

12. The process of claim 7 wherein the temperature is chosen from 35 to 50° C. and the pressure of hydrogen is chosen from 10 to 20 bar and Raney nickel is introduced in a weight ratio of from 1 to 20% with respect to the compound of general formula (II).

13. A process for the preparation of a 2-aminomethylpyridine derivative of general formula (I)



wherein

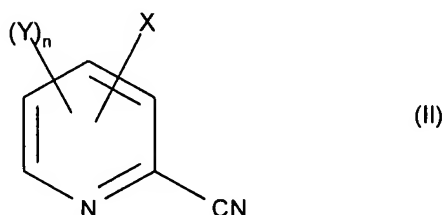
n represents 0, 1, 2 or 3,

X is a halogen atom,

each Y, which may be the same or different, is selected from the group consisting of a halogen atom, halogenoalkyl, alkoxycarbonyl, and alkylsulphonyl, or a salt thereof;

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comprising hydrogenating a 2-cyanopyridine derivative of general formula (II):



in which n, X, and Y are as described above,

in acetic acid using Raney nickel, at a temperature of from 30°C to 70°C, under a hydrogen pressure of from 10 to 20 bar.

14. A process for the preparation of 2-aminomethyl-3-chloro-5-trifluoromethylpyridine comprising hydrogenating 3-chloro-2-cyano-5-trifluoromethylpyridine in acetic acid using Raney nickel introduced in a weight ratio of from 1 to 20% with respect to the 3-chloro-2-cyano-5-trifluoromethylpyridine, at a temperature of from 40 to 50°C, under a hydrogen pressure of from 15 to 20 bar.

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**Evidence Appendix**

The Appellant does not submit any further evidence pursuant to 37 C.F.R. §§ 1.130, 1.131, or 1.132.

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**Related Proceedings Appendix**

No decisions rendered by a court or the Board in any proceeding identified pursuant to 37 C.F.R § 41.38(c)(1)(ii) are known to the Appellant.